

REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 24, 27, 28 are requested to be cancelled. Claims have been cancelled to advance the prosecution of the application.

Claim 33 is currently being amended. Amended claim 33 is rewritten as an independent claim. No new matter is introduced.

I. REJECTION UNDER 35 U.S.C. § 112.

Claim 33 is rejected under 35 U.S.C. § 112, first paragraph, for a lack of enablement. Applicants enclose with this communication a copy of Budapest Treaty Deposit Form indicating that a deposition of the cell line MSH2/9 under number RH532 was made on March 16, 2005, at ATCC Depository. Also enclosed is an affidavit by Hein Te Riele stating that the cell lines were deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent. Applicants believe that the deposition of the cell line obviates the rejection and, therefore, request withdrawal of the rejection.

II. REJECTION UNDER 35 U.S.C. § 103.

Claims 24, 27, 28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Varlet *et. al.*, Genbank accession number X81143, and Berns *et. al.* (US Patent 5,789,215 or WO 93/04169) in view of Orth *et. al.* (PNAS, 1994). In the present communication, applicants cancel claims 24, 27, 28 without prejudice to advance the prosecution of the application.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 33-49 are now pending in this application.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date

April 22, 2005

By

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BUDAPEST TREATY DEPOSIT FORM (BP/1)

American Type Culture Collection
P.O. Box 1548
Manassas, VA 20108

TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF THE BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF A PATENT PROCEDURE

ALL QUESTIONS MUST BE COMPLETED IN ENGLISH. PLEASE USE ONE FORM FOR EACH STRAIN DEPOSITED.

1. Name of deposit. Please mark the appropriate box and provide the information requested for the material.

- ☒ Microorganism - the complete scientific name including genus and species plus the source of the material
☐ Virus - the name, whether plant or animal, and source including geographic location
☒ Cell line - the species and tissue of origin, geographical source of isolation, and any known associated hazards (HIV, EBV, etc.)
☐ Genotype material - the name of organism from which vector, clone or library is derived, the source of the DNA insert identified by species (e.g., human, mouse) or scientific name, the name of gene, and the identity of the host organism
☐ Consortium or mixed culture - the identity of each component of the mixture
☐ Seeds, embryos, insect eggs, etc. - the common name, the scientific name of the source of the deposit, and geographical source

Human embryonic stem cells with a disruption in the D5H2 gene. Genotype: D5H2^{-/-}; Name: D5H2-9

2. Strain designation* (i.e., number, symbols, etc.) RH532

*The strain designation must correspond with the label.

3. Is this an original deposit under the Budapest Treaty? ☒ Yes ☐ No

4. Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty?

☐ Yes ☒ No

If yes, please indicate ATCC designation _____

5. Is this deposit a mixture of microorganisms or cells? ☐ Yes ☒ No

If yes, please describe. _____

6. Provide details necessary to cultivate, test for viability and store the deposit. If a mixture, provide description of components and a method to check for presence. If a plasmid, provide name of host and antibiotic resistance.

Cells can be grown on gelatin-coated tissue culture surfaces in complete medium = α -MEM + 10% FCS + LIF (10³ U/ml) (complete medium = α -MEM + 10% FCS + Na-pyruvate 150 μ M + non-essential amino acids)

7. Provide sufficient description so that ATCC may confirm deposit properly (e.g., Gram negative rod)

a. If deposit is a cell culture, is it being cultured in the presence of antibiotics? ☐ Yes ☒ No

If yes, please list the antibiotics: _____

b. If deposit is a hybridoma, what is the isotype of the antibody produced? _____

8. Safety: Is this strain hazardous to humans? NO Animals? NO Plants? NO

If yes, what is the recommended biosafety level for working with this strain? _____

(Refer to Biosafety in Microbiological and Biomedical Laboratories, 4th ed. HHS Publication No. (CDC) 83-8395, U.S. Department of Health and Human Services, Centers for Disease Control, Washington, DC, U.S. Government Printing Office, 1989. The entire text is available online at www.cdc.gov/od/ohrt/biosafety/biosafety.htm)



9. Regulatory Compliance:

- a. Was the material derived from a human? ☐ Yes ☒ No
If yes, was an IRB-approved consent form (human subjects) obtained? ☐ Yes ☐ No
- b. Was this material obtained from wildlife? ☐ Yes ☒ No
If yes, please indicate genus and species and whether wild or captive bred. _____
- c. Is work performed at your facility with exotic viruses affecting livestock and avian species? ☐ Yes ☒ No
- d. Identify any reagents of animal origin used to cultivate this organism/cell line (serum, growth factors, trypsin, etc.) and manufacturer, if known: Fetal Calf Serum

10. Availability:

Prior to issuance of a U.S. Patent, ATCC will only make a culture available as instructed by the depositor or relevant patent office. Samples must be provided to a specific investigator if a pertinent Patent Office under the Budapest Treaty instructs ATCC to do so. The following questions must be answered:

- a. As of date of deposit or conversion to meet the requirements of the Budapest Treaty, do you wish the deposit to be made available to anyone who requests a culture? If yes, there are no restrictions on distribution. Answering no will ensure the deposit is not available until the patent has issued. ☒ Yes ☐ No
- b. As of the date of deposit or conversion to meet the requirements of the Budapest Treaty, do you wish the deposit to be made available to requesters that satisfy Patent Offices in countries not signatory to the Budapest Treaty? ☒ Yes ☐ No
If "yes," please state which countries: All

Please note that if you are converting your deposit to meet the requirements of the Budapest Treaty, and your deposit has already been released for distribution due to the issuance of a U.S. Patent, you cannot restrict it from further distribution. After a U.S. Patent issues and we are so notified, ATCC makes the culture available to anyone who requests it, as allowed under U.S. Patent and Trademark Office (USPTO) Rules and Regulations (37 CFR 1.808 [a][2]).

11. Notification. ATCC will notify you of your ATCC number after viability of the deposit has been confirmed.

Name of individual to notify: Hein te Riele
Fax: 31206691383 Phone: 31205122084 E-mail: h.t.riete@nki.nl

12. Payment by check or credit card (MasterCard, VISA or American Express) must accompany the deposit unless prior arrangements for billing have been made and approved. ATCC accepts purchase orders for the exact amount.

Purchase Order No. _____ Check No. _____
Credit Card number _____ ☐ MasterCard ☐ VISA ☐ American Express
Exp. Date _____ Name shown on card: _____
(Please print clearly or type)
Signature of card holder: _____

PAYMENT: ATCC MUST HAVE A BILLING ADDRESS, CONTACT PERSON, PHONE AND FAX FOR ALL DEPOSITS:

Contact Name: _____
Billing Address: _____
Phone: (____) _____ Fax: (____) _____

Do you have a current ATCC account number? ☐ Yes ☐ No

If Yes, ATCC Account Number = _____

If No: To apply for an account with ATCC, please complete a New Account Application located on our Web site (www.atcc.org) and return it with supporting documentation to ATCC for approval.

USD 2500 has been transferred to ATCC, 007923990753, ABA 053001633
de Bank of America, Baltimore, MD, Federal ID 52-0196548
by Maxis France

13. Name, address, phone and fax number of your Attorney of Record

Prof. dr. Anton Berns, The Netherlands Cancer Institute
Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands
P: 31 20 512 1990 (Ref: Docket or Case No. _____)
F: 31 20 512 2011

14. **MUST BE COMPLETED.** Deposited on behalf of: (Verify with your management who owns the deposit. The owner is usually a company or institution, and not an individual.)

The Netherlands Cancer Institute / Antoni van Leeuwenhoek
Hospital

I understand and agree that the deposit may not be withdrawn by me for the period specified in Rule 9.1 of the Budapest Treaty (at least 30 years after the date of deposit or 5 years after the date of the most recent request for the deposit, whichever is longer), and that if a culture should die or be destroyed during the life of the patent, or the period of time so specified, it is my responsibility to replace it with a living culture of the same organism or cell. In the cases of viruses, cell cultures, plasmids, embryos, and seeds, it is my responsibility to supply a sufficient quantity for distribution for the period of time specified above.

S. Rodenhuys [Signature] 16/03/05
Printed Name Signature Date
Address: NKTI AVL Plesmanlaan 121 - 1066 CX Amsterdam NL
Phone: (020) 512 2870 Fax: (020) 512 2858 E-mail: stoden@ukinl

SHIPPING INFORMATION

BEFORE SHIPPING, PLEASE CONTACT THE ATCC PATENT DEPOSITORY FOR SHIPMENT ADVICE:

Fax: (703) 365-2745
E-mail: PatentDeposit@atcc.org

SHIPPING NOTICE:

The depositor is ultimately responsible for the shipment of deposits to ATCC and compliance with all applicable government regulations for the packaging and movement of the material. The depositor shall indemnify ATCC, to the extent permitted by law, against claims resulting from the violation of applicable government regulations caused by the depositor's shipment of deposits to ATCC.

STORAGE & FEES

Storage: Cultures are stored for 30 years from date of deposit or five years after the last request for a sample, whichever is longer, as required under the rules of patent offices in most countries.

Fees: All fees are subject to change. For current fees and other information, check our Web site at www.atcc.org or request a quotation of fees by e-mail at PatentDeposit@atcc.org or fax (703) 365-2745.

ATCC USE ONLY: ATCC DESIGNATION _____ REC'D _____ V.T. RESULT _____

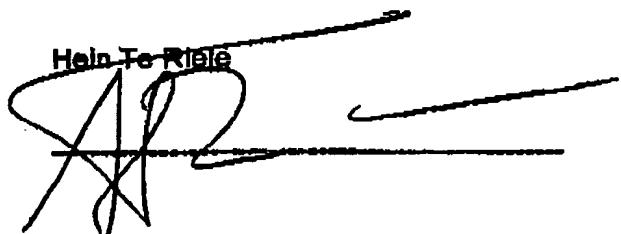
ATCC® is a registered trademark of the American Type Culture Collection.

Verification

I herewith verify that I have made a deposition of the cellline MSH2/9 (RH532) under the Budapest Treaty. I understand and agree that the deposit may not be withdrawn by myself for the period specified in Rule 9.1 of the Budapest Treaty (at least 30 years after the date of deposit or 5 years after the date of the most recent request for the deposit, whichever is longer), and that if a culture should die or be destroyed during the life of the patent, or the period of time so specified, it is my responsibility to replace it with a living culture of the same organism or cell. It is my responsibility to supply a sufficient quantity of the cellline for distribution for the period of time specified above.

I verify that all restrictions on the availability to the public of the cellline deposit will be irrevocably removed upon the granting of a patent from the above-identified application.

Hein Te Riele



Date:

080405